

C1
Conclude

signal peptides, as expected for secretory proteins. The length of the putative signal peptides was estimated after the analyses of the hydrophobicity plot, the predicted secondary structure and application of von Heijne's rule for the prediction of the most probable signal peptide cleavage site. The cleavage site for each subunit is shown in Table 2 by the asterisks. The correct prediction of the cleavage sites for S4 and S1 (unpublished) was confirmed by amino terminal sequencing of the purified mature subunits. The length of the signal peptides varies from 34 residues for S1, 28 residues for S3, and 27 residues for S2, to 21 residues for S4, and 20 residues for S5. All of the signal peptides contain a positively-charged amino terminal region of variable length, followed by a sequence of hydrophobic amino acids, usually in -helical or partially -helical, partially -pleated conformation. A less hydrophobic carboxy-terminal region follows, usually ending in -turn conformation at the signal peptide cleavage site. All subunits except S5 follow the -1, -3, rule, which positions the cleavage site after Ala-X-Ala. The amino-terminal charge for the subunit signal peptides varies between +4 for S1 and +1 for S4 and S5. All described properties correspond very well to the general properties for bacterial signal peptides.

IN THE CLAIMS

Please amend and replace the claim as follows:

C2

5. (amended) A method of producing a polypeptide, said polypeptide comprising at least a portion of mature S1 subunit of *B. pertussis* toxin, including position 9 of the mature S1 subunit of SEQ ID NO: 6, which exhibits substantially reduced ADP ribosyltransferase activity compared to wild-type *B. pertussis* toxin, wherein said polypeptide comprises an epitope reactive with a protective antibody against *B. pertussis* toxin and comprises an amino acid at position 9 of said mature S1 subunit of *B. pertussis* toxin other than arginine, said method comprising the steps of:

- expressing the polypeptide from DNA encoding the polypeptide; and
- isolating the polypeptide.

REMARKS

Applicant respectfully requests favorable reconsideration in view of the herewith presented amendments and remarks.